Paper No. 23

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte CHARLES T. ESMON
and PHILIP C. COMP

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Appeal No. 1997-3951
Application 08/238,987

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ON BRIEF

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Before WILLIAM F. SMITH, SPIEGEL, and ADAMS, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 18. Subsequent to the final rejection, claims 2 and 9 were canceled.

From the Advisory Action mailed August 29, 1995 (Paper No. 16), and the fact that

claims 6 and 12 are not rejected in the Examiner's Answer, it appears that the examiner has withdrawn the rejection as to these two claims and accordingly, they are no longer subject to this appeal.

Claims 1, 6, 8, and 12 are representative of the subject matter encompassed by the pending claims and read as follows:

1. A composition for inhibition of tumor growth in a non-murine patient comprising:

a pharmaceutical carrier containing an effective dosage of a compound specifically blocking the Protein C anti-coagulation system selected from the group consisting of anti-protein C antibodies, anti-protein S antibodies, inactivated protein C and C4b binding protein in combination with a compound eliciting production of cytokine in the patient, wherein the combination is in an effective dosage to cause hemorrhagic necrosis of the tumor and the dosage of the compound eliciting production of cytokine in the combination is not effective in the absence of the Protein C blocking compound.

6. The composition of claim 1 wherein the compound eliciting production of cytokines is endotoxin in a dosage stimulating production of tumor necrosis factor.

8. A method for inhibition of tumor growth in a patient comprising:

administering to a patient in need of treatment a compound specifically blocking the Protein C pathway, wherein the compound is not a cytokine selected from the group consisting of anti-protein C antibodies, anti-protein S antibodies, inactivated protein C and C4b binding protein, in a dosage blocking the Protein C anti-coagulation system and facilitating hemorrhagic necrosis of tumors, in combination with a compound eliciting production of cytokines, wherein the compound is not administered in a dosage effective to elicit hemorrhagic necrosis of the microvasculated solid tumors.

12. The method of claim 8 wherein the compound eliciting production of cytokines is endotoxin in a dosage stimulating production of tumor necrosis factor.

Claims 1, 3 through 5, 7, 8, 10, 11, and 13 through 18 stand rejected under 35 U.S.C. § 112, first paragraph (enablement). The examiner does not rely upon any evidence in support of this rejection. We reverse and make a new ground of rejection under 37 CFR § 1.196(b).

DISCUSSION

Parent application 07/389,617 issued as U.S. patent 5,147,638 (`638 patent). Claims 1 and 12 of the `638 patent read as follows:

1. A composition for inhibition of tumor growth in a patient comprising:

a pharmaceutical carrier containing a compound to block the protein C anticoagulation system selected from the group consisting of anti-protein C antibodies, anti-protein S antibodies, inactivated protein C and C4b binding protein in combination with a cytokine selected from the group consisting of tumor necrosis factor and a cytokine eliciting expression of tumor necrosis factor, wherein the combination is in an effective dosage to cause hemorrhagic necrosis of the tumor and the dosage of the cytokine in the combination is not effective in the absence of the protein C blocking compound.

12. A method for inhibition of tumor growth in a patient comprising: administering to a patient having a tumor a compound specifically blocking protein C, wherein the compound is not a cytokine, in a dosage blocking the Protein C anticoagulation system and facilitating hemorrhagic necrosis of microvasculated solid tumors.

As can be seen, composition claim 1 of the `638 patent requires the presence of "a cytokine selected from the group consisting of tumor necrosis factor and a cytokine eliciting expression of tumor necrosis factor," while composition claim 1 on appeal in relevant part requires "a compound eliciting production of cytokine in the patient."

The examiner's enablement rejection revolves around that portion of the claimed subject matter directed to "a compound eliciting production of cytokine in the patient." The examiner's reasoning in support of the rejection appears on pages 3 and 4 of the Examiner's Answer as follows:

> The claims encompass any compound which elicits production of any cytokine. The scope of the claims is not commensurate with the evidence of enablement provided by the disclosure with regard to the extremely large number of compounds and cytokines broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. The evidence of record is limited to a combination of TNF with a protein C blocking antibody or a combination of endotoxin with a protein C blocking antibody. There is no evidence of record in this application with respect to any other cytokines or any other compounds which broadly elicit production of any cytokine. In view of the diverse biological activities of the cytokines and the cytokine network there is a reasonable doubt that any compound which elicits production of any cytokine would be effective in tumor therapy as claimed.
>
> Thus, Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed composition in a manner reasonably correlated with the scope of the disclosure. The scope of the claims must bear a reasonable correlation with the scope of

> enablement. Without sufficient guidance, experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. The statement of the rejection is conclusory in nature and does not reflect

that the rejection is premised upon the correct legal standards. To the extent the rejection is based upon "undue experimentation" we point to the courts' statement in PPG Indus. Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996) that:

> In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. See, e.g., In re Goodman, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993); Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d. 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991); In re Vaeck, 947 F.2d at 496, 20 USPQ2d at 1445. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of Appeals summarized the point well when it stated:
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> > The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

Our appellate reviewing court has also indicated in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988):

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd.Pat.App. & Int. 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (footnote omitted).

In concluding that appellants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed invention, the examiner has not taken into account on this record the disclosure at page 23 of the specification wherein appellants instruct:

> The Protein C blocking agent is prefereably administered in combination with a cytokine that stimulates natural killer and lymphokine-activated killer cell-mediated cytotoxicity, activates macrophages, stimulates Fc receptor expression on mononuclear cells and antibody-de[pendent cellular cytotoxicity, enhances HLA class II antigen expression, and/or stimulates procoagulant activity, such as tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-2 (IL-2), gamma interferon (gamma-IFN), or granulocyte-macrophage colony stimulating factor (GMCSF). Alternatively, an agent such as endotoxin, or the purified liposaccharide (LPS) from a gram negative bacteria such as E. coli, can be used to elicit

production of cytokines such as TNF. Recombinant TNF, IL-2 and GMCSF can be obtained from Cetus Corporation, 1400 53rd Street, Emeryville, CA, or Biogen corp. [sic, Corp.], Cambridge, MA. IL-1 can be obtained can be obtained [sic] from Genentech, South San Francisco, CA, or Hoffman-LaRoche, Nutley, NJ. Gamma interferon can be obtained from Genentech, Biogen or Amgen Biologicals, Thousand Oaks, CA. LPS from E. coli, strain 055:B5 can be obtained from Difco, Detroit, MI.

Clearly, under the legal standards set forth above, the examiner needs to conduct certain fact finding before concluding that the claims are non-enabled. That fact finding has not been performed. Furthermore, the specification does provide guidance as to the type of cytokines which are useful in the present invention, both by function and specific compounds.

The examiner has not adequately explained why one skilled in the art would have undue difficulty in identifying compounds which elicit production of such cytokines as required by the claims on appeal.

The other aspect of the examiner's position is his concern that the "claims broadly encompass a significant number of inoperative species." However, the examiner has not favored the record with any specific examples of such "inoperative species." As set forth in Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576-77, 224 USPQ 409, 414 (Fed. Cir. 1984):

> Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. "It is not a function of the claims to specifically exclude . . . possible inoperative substances . . . .

> In re Dinh-Nguyen, 492 F.2d 856, 859-59, 181 USPQ 46, 48 (CCPA 1974) (emphasis omitted). Accord, In re Geerdes, 491 F.2d 1260, 1265, 180 USPQ 789, 793 (CCPA 1974); In re Anderson, 471 F.2d 1237, 1242, 176 USPQ 331, 334-35 (CCPA 1971). Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid. See, e.g., In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971).

Suffice it to say, the examiner has not explained why the number of "inoperative species" is so significant that practice of the claim throughout its scope would require undue experimentation.

The rejection of the claims under 35 U.S.C. § 112, first paragraph (enablement) is reversed.

NEW GROUND OF REJECTION UDNER 37 CFR § 1.196(b)

Under the provisions of 37 CFR § 1.196(b), we make the following new ground of rejection.

Claims 1, 3 through 8 and 10 through 18, all the claims pending in the application, are rejected under the judicially created grounds of obviousness-type double patenting over the claims of the `638 patent.

At the time of the final rejection, all pending claims stood rejected on obviousness-type double patenting grounds on the basis of the claims of the `638 patent. See Paper No. 14, page 5. Therein, the examiner acknowledged

appellants' "intent to file a terminal disclaimer." See also appellants' submission on August 9, 1995 (Paper No. 15), page 7 "Applicants are willing to file a terminal disclaimer in accordance with 37 CFR § 1.321(b) . . . ." From the Advisory Action, it appears the examiner withdrew the enablement rejection in regard to claims 6 and 12 on the basis of the proferred terminal disclaimer. For reasons not apparent from this record, the examiner did not repeat and maintain the obviousness-type double patenting rejection in the Examiner's Answer. We do not find any indication in the record that the examiner intended to withdraw the rejection with the thought that appellants need not file a terminal disclaimer.

In making this new ground of rejection, we are only restoring the record to the state in which it was prior to this appeal, i.e., all the claims stand rejected on obviousness-type double patenting grounds on the basis of the claims of the `638 patent. As noted, appellants have acquiesced in this rejection.

TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 CFR § 1.196(b)(amended effective Dec. 1, 1997, by final rule notice, 62 Fed. Reg. 53,131, 53,197 (Oct. 10, 1997), 1203 Off. Gaz. Pat. & Trademark Office 63, 122 (Oct. 21, 1997)). 37 CFR § 1.196(b) provides that, "A new ground of rejection shall not be considered final for purposes of judicial review."

37 CFR § 1.196(b) also provides that the appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (§ 1.197(c)) as to the rejected claims:

> (1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner. . . .
>
> (2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED
37 CFR § 1.196(b)

William F. Smith)
Administrative Patent Judge)
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)
) BOARD OF PATENT

Carol A. Spiegel)
Administrative Patent Judge) APPEALS AND
)
) INTERFERENCES
)
Donald E. Adams)
Administrative Patent Judge)

WFS/cam

Patrea L. Pabst
Arnall, Golden & Gregory
2800 One Atlantic Center
1201 West Peachtree Street
Atlanta, GA 30309-3400